Exhibit D

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ORIGINAL ARTICLE

Histopathology of excised midurethral sling mesh

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Abstract
Introduction and hypothesis The objective of this study was to compare the histological characteristics of pathological specimens of excised midurethral sling mesh and surrounding vaginal tissue in patients who presented preoperatively with pain and/or exposure of mesh to patients who underwent mesh excision for voiding dysfunction without pain and/or erosion.
Methods This is a retrospective case–control study of women who underwent excision of midurethral sling mesh between 2008 and 2013. Three groups were identified: (1) voiding dysfunction without pain or exposure (control group), (2) pain and/or mesh exposure, and (3) voiding dysfunction with pain and/or mesh exposure. All original pathological specimens were rereviewed by one pathologist blinded to indication for excision and the previous pathology report. Degree of inflammation and fibrosis were recorded based on a 4-point scale along with the presence of giant cell reaction.
Results A total of 130 subjects met inclusion criteria: 60 (46.2 %) with voiding dysfunction only, 21 (16.2 %) with pain/erosion, and 49 (37.7 %) with both pain/exposure and voiding dysfunction. The voiding dysfunction only group was found to have significantly higher levels of inflammation, median grade 2 (1–3), compared to the other two groups with a p value of 0.007. There were no statistical differences in fibrosis and giant cell reaction between the three groups.
Conclusions Midurethral sling mesh excised for voiding dysfunction demonstrates elevated levels of inflammation compared to mesh that is excised for pain and/or exposure. The vaginal tissue fibrosis and giant cell reaction are similar in patients who undergo mesh excision for voiding dysfunction and pain, and/or mesh exposure.

Keywords Foreign body reaction · Mesh erosion · Mesh exposure · Midurethral sling · Vaginal mesh

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Introduction

Known complications of a midurethral sling placement include bladder, bowel, and vascular injury as well as postoperative voiding dysfunction and mesh erosion or exposure [1]. Review of the literature shows that the risk of mesh exposure/erosion after midurethral sling placement ranges from 0.3 to 5.9 % [2–4]. Risk factors associated with mesh exposure/erosion include younger age at time of placement [5], concomitant prolapse surgery [5], and certain synthetic mesh materials [6, 7].

Following the 2008 and 2011 US Food and Drug Administration (FDA) Safety Communication reports on transvaginal mesh use, reported complications of mesh erosion/exposure have increased significantly [8]. As a result, there has been a growing focus on the biomechanics and physical properties of different types of vaginal mesh [9], and efforts to identify patient-centered risk factors for mesh erosion have also increased. Despite these efforts, limited research has been performed on the human host response to synthetic midurethral slings. This is surprising, as research exists on other types of synthetic materials used in surgery. For example, in 1954, Marlex mesh was introduced for abdominal hernia repairs [10], and due to postoperative complications associated with its use numerous research studies were conducted to compare different types of mesh materials and